Amendment

In the Specification

Please insert the following heading on page 1, after the title and before line 3.

BACKGROUND OF THE INVENTION

Please insert the following heading on page 2, line 3.

BRIEF SUMMARY OF THE INVENTION

Please insert the following heading on page 4, line 9.

DETAILED DESCRIPTION OF THE INVENTION

Please insert the following heading on page 4 after line 8 and before the heading "**DETAILED DESCRIPTION OF THE INVENTION**".

BRIEF DESCRIPTION OF THE DRAWINGS

Please insert the following paragraphs on page 4 after the heading "**BRIEF DESCRIPTION OF THE DRAWINGS**" and before the heading "**DETAILED DESCRIPTION OF THE INVENTION**".

Figure 1 shows that chronic wasting disorders show increased activity of SNS (sympathetic nervous system) as evidenced by increased plasma noradrenaline levels. All of the cachectic disorders marked (*) have mean plasma noradrenaline levels which are higher than normal. Mean values are given for noradrenaline plasma levels in nmol/l. COPD is chronic occluded pulmonary disease. ncCHF is non-cachectic CHF.

Figure 2 shows that, on average, patients with active wasting disease have 2.5- to 12-fold increased aldosterone levels compared to healthy controls (their mean:43.2 ng/ml, upper limit or normal:81 ng/ml). Patients with weight loss due to malnutrition have normal aldosterone levels.

Please replace the paragraph on page 20, lines 24-25, with the following paragraph.

~~Figure 1~~ Table 1 shows individual data for noradrenaline plasma levels which is summarised in Figure ~~2~~ 1.

Please delete the paragraph on page 20, line 27 to page 21, line 2.

Please delete the paragraph on page 21, lines 4–7.

Please delete the paragraph on page 21, lines 9-10.

Please delete the paragraph on page 21, lines 12-14.

Please replace the paragraph on page 27, line 25 to page 28, line 9, with the following paragraph.

We have studied a variety of other cachectic conditions - for instance due to AIDS, liver cirrhosis, chronic obstructive pulmonary disease, chronic renal failure, chronic infections (like pneumonia) and cancer - and we have found activation of the SNS as evidenced by elevated plasma noradrenaline levels (mean plasma levels were clearly above the upper limit of the normal range, see ~~Figures 1 and 2~~ Table 1 and Figure 1). This is not dependent on any specific etiology for the cachectic disorder, in fact we find elevated noradrenaline plasma levels (ie SNS activity) also in cases of idiopathic cachexia, ie cachexia of unknown origin. Nevertheless, we find the activation of the SNS to be specific for cachectic disorders, as it is not seen in patients with a similar degree of weight loss consequent upon malnutrition.

Please insert the following table on page 28, line 23.

TABLE 1

ANOVA Table for NA* nmol/l

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Cachexia diag.-NA-Figure	11	260.240	23.658	2.850	.0020
Residual	103	825.866	8.019		

Model II estimate of between component variance: 1.796
94 cases were omitted due to missing values.

Means Table for NA* nmol/l
Effect: Cachexia diag.-NA*-Figure

	Count	Mean	Std. Dev.	Std. Err.
AIDS	6	5.217	4.801	1.960
cachectic CHF	15	4.870	2.518	.650
Cancer	2	8.365	5.056	3.575
chronic renal failure	2	3.686	4.688	3.315
COPD	14	3.643	2.305	.616
healthy controls	16	1.940	.687	.172
ideopathic cachexia	2	3.835	3.203	2.265
infection	6	6.437	6.966	2.844
Livercirrh + Cachexia	6	6.098	5.693	2.324
Malnutrition	5	2.967	1.764	.728
more Controls	3	2.373	1.088	.634
nc CHF	37	2.684	1.344	.221

Fisher's PLSO for NA* nmol/l
Effect: Cachexia diag.-NA*-Figure
Significance Level: 5%

	Means Diff.	Crit. Diff.	P-Value
AIDS, cachectin CHF	.347	2.718	.8004
AIDS, Cancer	-3.148	4.586	.1768
AIDS, chronic renal failure	1.522	4.586	.5118
AIDS, COPD	1.574	2.740	.2579
AIDS, healthy controls	3.277	2.688	.0174
AIDS, ideopathic cachexia	1.382	4.586	.5514
AIDS, infection	-1.220	3.249	.4572
AIDS, Livercirrh + Cachexia	-.882	3.243	.5909
AIDS, Malnutrition	2.230	3.249	.1756
AIDS, more Controls	2.643	3.971	.1586
AIDS, nc CHF	2.693	2.472	.0371
cachectic CHF, Cancer	-3.495	4.228	.1042
cachectic CHF, chronic renal failure	1.175	4.226	.5827
cachectic CHF, COPD	1.227	2.087	.2462
cachectic CHF, healthy controls	2.930	2.018	.0049
cachectic CHF, ideopathic cachexia	1.095	4.228	.6283
cachectic CHF, infection	-1.667	2.713	.2547
cachectic CHF, Livercirrh + Cachexia	-1.228	2.713	.3713
cachectic CHF, Malnutrition	-1.869	2.713	.1716
cachectic CHF, more Controls	2.497	3.552	.1663
cachectic CHF, nc CHF	2.286	1.719	.0096
Cancer, chronic renal failure	4.670	5.616	.1022
Cancer, COPD	4.722	4.246	.0296
Cancer, healthy controls	6.425	4.212	.0031
Cancer, ideopathic cachexia			
Cancer, infection	1.928	4.586	.4062
Cancer, Livercirrh + Cachexia	2.267	4.586	.3292
Cancer, Malnutrition	5.378	4.586	.0220
Cancer, more Controls	5.992	5.127	.0224
Cancer, nc CHF	5.781	4.077	.0058
chronic renal failure, COPD	.052	4.246	.9805
chronic renal failure, healthy controls	1.755	4.212	.4105
chronic renal failure, ideopathic cachexia	-.140	5.516	.9607
chronic renal failure, infection	-2.742	4.586	.2384
chronic renal failure, Livercirrh + Cachexia	-2.403	4.586	.3010
chronic renal failure, Malnutrition	.708	4.586	.7600

chronic renal failure, more Controls	1.322	5.127	.6109
chronic renal failure, nc CHF	1.111	4.077	.5900
COPD, healthy controls	1.703	2.066	.1085
COPD, ideopathic cachexia	-.192	4.246	.9285
COPD, Infection	-2.794	2.740	.0456
COPD, Livercirrh + Cachexia	-2.456	2.740	.0785
COPD, Malnutrition	.856	2.740	.6360
COPD, more Controls	1.269	9.573	.4827
COPD, nc CHF	1.059	1.762	.2362
healthy controls, ideopathic cachexia	-1.895	4.212	.3743
healthy controls, infection	-4.497	2.689	.0013
healthy controls, Livercirrh + Cachexia	-4.158	2.689	.0028
healthy controls, Malnutrition	-1.047	2.689	.4418
healthy controls, more Controls	-.433	3.533	.8083
healthy controls, nc CHF	-.644	1.680	.4491
ideopathic cachexia, infection	-2.602	4.586	.2631
ideopathic cachexia, Livercirrh + Cachexia	-2.263	4.586	.3299
ideopathic cachexia, Malnutrition	.846	4.586	.7144
ideopathic cachexia, more Controls	1.462	6.127	.5730
ideopathic cachexia, nc CHF	1.251	4.077	.5441
infection, Livercirrh + Cachexia	.388	3.243	.8366
infection, Malnutrition	3.450	3.243	.0373
infection, more Controls	4.068	3.971	.0450
infection, nc CHF	3.853	2.472	.0026
Livercirrh + Cachexia, Malnutrition	3.112	3.243	.0598
Livercirrh + Cachexia, more Controls	3.725	3.971	.0657
Livercirrh + Cachexia, nc CHF	3.515	2.472	.0058
Malnutrition, more Controls	.613	3.971	.7600
Malnutrition, nc CHF	.403	2.472	.7472
more Controls, nc CHF	-.210	3.371	.9017

* NA is noradrenaline.

Please replace the paragraph on page 29, lines 4-14, with the following paragraph.

Aldosterone serum levels have been analysed in a number of subjects with these disorders compared to healthy controls, patients with weight loss due to malnutrition (ie no

active wasting disease), and CHF patients without cachexia (see Table below and Figure ~~3~~ 2). Patients with active wasting disease have on average 2.5 to 13-fold increased aldosterone levels compared to healthy control subjects (their mean: 43.2 ng/ml, upper limit or normal: 81 ng/ml). Patients with weight loss due to malnutrition have normal aldosterone levels. This supports our view that high aldosterone levels are pathophysiologically linked to the presence of chronic active body wasting due, ie cachexia, and that treatment with aldosterone antagonists may be beneficial.

Please delete the paragraphs from page 40, line 21 to page 51, line 3.

Please replace the paragraph on page 51, lines 5-6, with the following paragraph.

Example ~~10~~ 6: The presence of sympathetic nervous system activation and abnormal sympatho-vagal balance in AIDS - related wasting disease.

Please replace the paragraph on page 53, lines 18-19, with the following paragraph.

Example ~~11~~ 7: Treatment of a cachectic patient with chronic heart failure with an example beta-blocker (carvedilol).

Please replace the paragraph on page 55, lines 17-18, with the following paragraph.

Example ~~12~~ 8: Treatment of cachexia patients with an aldosterone antagonist (spironolactone).